UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/434,382	11/05/1999	SEAN V. TAVTIGIAN	2318-247	3879

7590 01/02/2002

JEFFREY L IHNEN
ROTHWELL FIGG ERNST & KURZ
SUITE 701 EAST
555 13TH STREET NW
WASHINGTON, DC 20004

EXAMINER	
HUNT, JENNIFER ELIZABETH	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/434,382	Applicant(s) Tavtigian et al.
	Examiner Jennifer Hunt	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 26, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 10-25, and 27-78* is/are pending in the application.

4a) Of the above, claim(s) *16-24 and 27-60* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 11-15, 61-63, and 67-77* is/are rejected.

7) ☒ Claim(s) *10, 25, 64-66, and 78* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Response to Amendment

1. Acknowledgment is made of applicant's cancellation of claims 4-9 and 26, and addition of new claims 61-78. Claims 1-3, 10-25, 27-78 are pending in the application. Claims 16-24 and 27-60 have been withdrawn from consideration by the examiner, as they are drawn to a non-elected invention. Claims 1-3, 10-15, 25, and 61-78 are addressed herein.

Claim Objections/Rejections Withdrawn

2. All rejections of claims 4-9 and 26 are withdrawn in light of the cancellation thereof.

3. The objection to claim 1 for containing a typographical error is withdrawn in light of the amendments thereto.

4. The rejection of pending claims 1-3, 10-15 and 25 as improper because they use the abbreviation HPC2, without identifying which HPC2 they refer to is withdrawn in light of the amendments thereto.

5. The rejection of pending claims 1-3, 10-15 and 25 as being unclear in the recitation of "a modified form which is functionally equivalent" is withdrawn in light of the amendments thereto.

6. The rejection of pending claim 2 as unclear in the recitation of stringent conditions is withdrawn in light of the amendments thereto.

7. The rejection of pending claim 2 as unclear in the recitation of "corresponding RNA" is withdrawn in light of the amendments thereto.

8. The rejection of pending claim 10 as unclear in the recitation of "said nucleic acid" is withdrawn in light of the amendments thereto.

9. The rejection of pending claim 12 for having insufficient antecedent basis is withdrawn in light of the amendments thereto.

10. The rejection of pending claim 12 as unclear in the recitation of "capable of directing the expression" is withdrawn in light of the amendments thereto.

11. The rejection of pending claim 25 as unclear in the recitation of "derived from" is withdrawn in light of the amendments thereto.

12. The rejection of pending claims 1-3 and 11-15 under 35 U.S.C. 112, first paragraph, the written description rejection, is withdrawn in light of the amendments thereto.

13. The rejection of pending claims 1-3 and 11-15 under 35 U.S.C. 112, first paragraph, the enablement rejection, is withdrawn in light of the amendments thereto.

14. The rejection of pending claim 2 under 35 U.S.C. 102(a) as being anticipated by Accession AC005277, IDS AN is withdrawn in light of the amendments thereto.

15. The rejection of pending claim 25 under 35 U.S.C. 102(b) as being anticipated by Ohagi et al., PNAS, Vol. 89, pages 4977-4981 is withdrawn in light of the amendments thereto.

16. The rejection of pending claims 2 and 25 under 35 U.S.C. 103(a) as being unpatentable over Accession AC005277, IDS AN is withdrawn in light of applicant's arguments and amendments thereto.

Claim Rejections Maintained

17. The rejection of claims 10 and 25 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (the written description rejection) is maintained for reasons of record, and is applied to newly added claims 64-66 and 78.

Claims 10, 25, 64-66 and 78 are broadly drawn nucleic acids of any size, including mutants, modified forms, and variants thereof, which contain a part of SEQ ID NO: 1, or the nucleic acid sequence encoding SEQ ID NO:2. The claims are drawn to a polynucleotide of any size which is only defined by a small number of nucleic acid resides, hence the claims are drawn to nucleic acid sequences which minimally contain only portions of SEQ ID NO:1, or the nucleic acid sequence encoding SEQ ID NO:2. Thus the claims are drawn to a large genus of molecules. In the case of small identified nucleic acid sequences claimed with open language, the genus of the polynucleotides comprising a partial sequence encompasses a variety of subgenera with widely varying attributes. The specification discloses only the structural features of one species,

the polynucleotide of SEQ ID NO:1 and the polypeptide of SEQ ID NO: 2, which is encoded by SEQ ID NO:1.

Thus the specification lacks information to lead one of ordinary skill in the art to understand that the applicant had possession of the broadly claimed genus of polynucleotides at the time the instant application was filed.

Applicant argues that the amendments overcome the rejection. Applicant's arguments filed 10-02-2001 have been fully considered but they are not persuasive.

This is not persuasive because the claims still broadly recite fragments as small as 8 or 13 nucleic acids in length, claimed with open language, and thus still encompass a broad genus of molecules.

18. The rejection of claims 10 and 25 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (the enablement rejection) is maintained for reasons of record, and is applied to newly added claims 64-66 and 78.

As set forth in the previous Office Action, factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the

predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims are broadly drawn to polynucleotides of virtually any size, provided that they share some sequence similarity with the polynucleotide encoding the HPC2 polypeptide of SEQ ID NO:2 or the polynucleotide of SEQ ID NO:1.

The specification teaches the polynucleotide of SEQ ID NO:1, derived from cDNA libraries screened for a Chromosome 17 mutation which correlates to an increased risk of prostate cancer. The specification teaches an open reading frame for the polypeptide, as well as the exonic and intronic sections, theoretical methods of expression, and production of antibodies to portions of the polypeptide. There is a prophetic example of gene analysis (Example 8), but this example is merely an invitation/wish list for future experimentation and provides no information about the gene beyond what is summarized above.

Thus the claims are broadly drawn to literally almost any polynucleotide, provided that it has minimal correlation to the polynucleotide encoding SEQ ID NO:2 , or to SEQ ID NO:1. Further, it is well established in the art that predicting the how alterations, mutations, modifications of a polynucleotide will affect the encoded polypeptide is difficult and unpredictable, and well out of the realm of routine experimentation.

For example, Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to

function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput

computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3).

Further, the disclosure of one HPC2 polynucleotide which presumably encodes the corresponding polypeptide is insufficient support under the first paragraph of 35 U.S.C 112 for claims which encompass any and all HPC2 polynucleotides and fragment, provided that they minimally have 8 or 13 nucleotides in common. The courts have held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based In some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not In compliance with the first paragraph of U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill In the art; In cases involving predictable factors, such as

> mechanical or electrical elements, a single embodiment provides broad enablement In the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; In cases involving unpredictable factors, such as chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

Thus for the reasons set forth above, specifically, because of the large breadth of the claims, the limited guidance provided in the specification, the relative lack of predictability and skill of those in the art with regard to determining how alteration of nucleic acid sequences corresponds to protein structure and function, one of skill in the art would not be enabled to make the invention.

Applicant argues that the amendments overcome the rejection. Applicant's arguments filed 10-02-2001 have been fully considered but they are not persuasive.

This is not persuasive because the claims still broadly recite fragments as small as 8 or 13 nucleic acids in length, claimed with open language, and thus still encompass a broad genus of molecules.

Conclusion

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Claims 1-3, 11-15, 61-63, 67-77 are allowed. Claims 10, 25, 64-66 and 78 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Hunt

December 30, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600